Recruitment of a contralateral head turning synergy by stimulation of monkey supplementary eye fields

Brendan B. Chapman, Michael A. Pace, Sharon L. Cushing, and Brian D. Corneil

1Graduate Program in Neuroscience and Departments of 2Physiology and Pharmacology and 3Psychology, University of Western Ontario, London; 4Department of Otolaryngology-Head and Neck Surgery, Hospital for Sick Children, University of Toronto, Toronto; and 5Centre for Brain and Mind, Robarts Research Institute, London, Ontario, Canada

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Chapman BB, Pace MA, Cushing SL, Corneil BD. Recruitment of a contralateral head turning synergy by stimulation of monkey supplementary eye fields. J Neurophysiol 107: 1694–1710, 2012. First published December 14, 2011; doi:10.1152/jn.00487.2011.—The supplementary eye fields (SEF) are thought to enable higher-level aspects of oculomotor control. The goal of the present experiment was to learn more about the SEF’s role in orienting, specifically by examining neck muscle recruitment evoked by stimulation of the SEF. Neck muscle activity was recorded from multiple muscles in two monkeys during SEF stimulation (100 μA, 150–300 ms, 300 Hz, with the head restrained or unrestrained) delivered 200 ms into a gap period, before a visually guided saccade initiated from a central position (doing so avoids confounds between initial position and prestimulation neck muscle activity). SEF stimulation occasionally evoked overt gaze shifts and/or head movements but almost always evoked a response that invariably consisted of a contralateral head turning synergy by increasing activity on contralateral turning muscles and decreasing activity on ipsilateral turning muscles (when background activity was present). Neck muscle responses began well in advance of evoked gaze shifts (~30 ms after stimulation onset, leading gaze shifts by ~40–70 ms on average), started earlier and attained a larger magnitude when accompanied by progressively larger gaze shifts, and persisted on trials without overt gaze shifts. The patterns of evoked neck muscle responses resembled those evoked by frontal eye field (FEF) stimulation, except that response latencies from the SEF were ~10 ms longer. This basic description of the cephalo-motor command evoked by SEF stimulation suggests that this structure, while further removed from the motor periphery than the FEF, accesses premotor orienting circuits in the brain stem and spinal cord in a similar manner.

oculomotor control; frontal cortex; head movements

THE MONKEY supplementary eye fields (SEF) are located in the dorso-medial frontal cortex. Anatomical studies suggest a role for the SEF in producing saccadic eye movements based on direct connections to premotor nuclei that control saccades, as well as connections to other oculomotor areas such as the frontal eye fields (FEF) and superior colliculus (SC) (Amiez and Petrides 2009; Shook et al. 1990, 1991). Consistent with this, microstimulation of the SEF reliably elicits contralateral saccades (Fujii et al. 1995; Huerta and Kaas 1990; Russo and Bruce 1993; Schall 1991a; Schlag and Schlag-Rey 1987; Tehovnik and Lee 1993). Recordings within the SEF have not only demonstrated sensory and motor signals (Russo and Bruce 1996, 2000; Schall 1991b) but also suggested a role for the SEF in numerous cognitive processes related to spatial selectivity, errors, representation of movement plan, ordinal position selectivity, reward value, and new stimulus-response associations (Berdyyeva and Olson 2010; Campos et al. 2009; Chen and Wise 1995; Coe et al. 2002; Fujii et al. 2002; Moorman and Olson 2007; So and Stuphorn 2010; Stuphorn et al. 2000). The current consensus is that the SEF, like other supplementary motor areas, serves as a critical interface between cognition and action (Nachev et al. 2008).

Although the SEF is well studied with the head restrained, a potential role for the SEF in head-unrestrained gaze shifts has only recently begun to be addressed. An early study showed that SEF stimulation did not reliably evoke head motion (Schlag and Schlag-Rey 1987), but more recent systematic explorations of this structure in monkeys have demonstrated that eye-head gaze shifts can be reliably evoked by SEF stimulation (Chen and Walton 2005; Martinez-Trujillo et al. 2003a, 2003b, 2004). These studies have demonstrated that the head can make a significant contribution to gaze shifts evoked from the SEF, doing so with kinematics that resemble those observed during volitional eye-head gaze shifts. Despite the head’s substantial inertia, which introduces an ~30- to 40-ms lag between neck muscle recruitment and the onset of head motion, head movements evoked from the SEF frequently start around the time of the gaze shift, sometimes even preceding gaze shift onset (Chen and Walton 2005). Depending on the initial position of the eyes and head, SEF stimulation can also evoke head-only movements directed away from the side of stimulation (Chen and Walton 2005). Finally, eye-head gaze shifts evoked from the SEF appear to be encoded in a variety of reference frames (Martinez-Trujillo et al. 2004), potentially indicating a role for the SEF in implementing arbitrary reference frame transformations.

This article is the first in a series of studies designed to provide further information about the contribution of the SEF to eye-head gaze shifts, with a specific focus on the cephalo-motor component. Here, we paired recordings of neck muscle activity with SEF stimulation, paralleling similar experiments performed in the FEF (Corneil et al. 2010; Elsley et al. 2007; Guitton and Mandl 1978), SC (Corneil et al. 2002a, 2002b; Guitton et al. 1980; Hadjidimitrakis et al. 2007; Roucoux et al. 1980), and interstitial nucleus of Cajal (INC) (Farshadmanesh et al. 2008). Pairing neck muscle recordings with SEF stimulation allows us to quantify the spatial (i.e., which muscles) and temporal aspects of neck muscle responses evoked by SEF stimulation, at a resolution surpassing what can be gained from examining the kinematics of evoked movements. To enable comparison with similar data obtained from the FEF and to...
reduce the confounding relationship between neck muscle activity and initial eye-in-head or head-on-body position (André-Deshays et al. 1988; Corneil et al. 2002a; Hadjimitrakis et al. 2007; Lestienne et al. 1984; Vidal et al. 1982; Werner et al. 1997), we delivered stimulation while monkeys were looking straight ahead, just prior to the requirement to make a visually guided saccade in one of eight possible directions. Similar to results obtained from the FEF (Elsley et al. 2007), we observed robust recruitment of a head turning synergy at almost all SEF sites. This recruitment reliably preceded gaze shift onset and persisted on trials where stimulation failed to evoke a gaze shift. Unlike the FEF, however, the latency of the evoked response was considerably longer than the conduction and synaptic delays of the shortest path to the motor periphery. Portions of this article have been presented in abstract form (Chapman et al. 2010).

RESULTS

Microstimulation parameters. Microstimulation was delivered through tungsten microelectrodes (0.5–1.2 MΩ at 1 kHz) lowered through a 23-gauge guide tube secured within a Delrin grid. Stimulation consisted of a train of biphasic stimulation pulses (cathodal first) delivered at a frequency of 300 Hz. Each individual pulse was 0.1 ms in duration, and the biphasic pulses were separated by 0.1 ms. First-order considered to automatically detect the beginning and end of gaze shifts and head movements with velocity thresholds of 30°/s (gaze) or 10°/s (head) and display the data. These markers could be changed by an analyst, who could also reject trials for other reasons (e.g., excessive EMG activity due to postural shifts or head shakess). Anticipatory movements (beginning <60 ms from target appearance) or movements that began >600 ms after target appearance onset were automatically discarded. Trials with gaze shifts occurring just before or <20 ms after stimulation onset were also rejected. Trials were rejected at a rate of <5%.

We performed a number of analyses on evoked neck EMG responses. For consistency with previous reports (Corneil et al. 2002a, 2002b; Elsley et al. 2007), we calculated mean EMG responses by aligning stimulation trials on the onset of stimulation. The mean and standard deviation of the background activity in the 100 ms preceding stimulation onset were calculated. The facilitation latency was determined as the first of five consecutive bins after stimulation onset in which the EMG activity was 2 standard deviations above the background activity. The peak magnitude of the EMG response was taken as the highest mean value during stimulation minus the average background activity. We also performed a second analysis to extract the onset of the neck EMG response on a trial-by-trial basis. The logic and derivation of this analysis are described below.

Stimulation was delivered throughout a large sampling of the dorso-medial frontal cortex in two monkeys (Fig. 1A). Saccades were reliably evoked from noncentral FP locations

METHODOLOGY

Subjects and surgical procedures. Two male monkeys (Macaca mulatta; monkeys S and Z) weighing 12–14 kg were used in this experiment. All training, surgical, and experimental procedures were conducted in accordance with Canadian Council on Animal Care policy on the use of laboratory animals and approved by the Animal Use Subcommittee of the University of Western Ontario Council on Animal Care. The monkeys’ health and weight were monitored daily by technicians and/or veterinarians at the university.

Each animal underwent two surgeries, the details of which have been described previously (Elsley et al. 2007). In the first surgery, we implanted a head post, a scleral search coil, and a recording cylinder positioned over a 19-mm craniotomy centered near midline over the frontal lobes to allow access to the SEF (interruption coordinates: monkey S: AP = 25.0, ML = 3; monkey Z: AP = 24.0, ML = 2). In the second surgery, we implanted chronically indwelling bipolar hook electrodes bilaterally in five pairs of neck muscles: obliquus capitis inferior (OCI), rectus capitis posterior major (RCP), splenius capitis (SP), biventer cervicis (BC), and complexus (COM) muscles. Anatomical and functional descriptions of these muscles have been provided previously (Corneil et al. 2001; Richmond et al. 2001b). OCI, RCP, and SP contribute primarily to horizontal head turns, while BC and COM primarily serve to pitch the head upward.

Microstimulation parameters. Microstimulation was delivered via a sipper tube that moved with the head. When head unrestrained, the monkey received a liquid reward via a sipper tube that moved with the head.

We identified SEF sites as those from which stimulation reliably evoked gaze saccades with a probability >50%, regardless of head restraint. Since the probability of an evoked saccade depends on initial position (Slagl and Slagl-Rey 1987), our initial identification of SEF stimulation sites used noncentral FP locations. Once a valid SEF site was identified, we ran the gap-saccade task described below with only a central FP. This was done to control for variation in background neck EMG activity with initial eye-in-head and/or head-in-space position (André-Deshays et al. 1988; Corneil et al. 2001, 2002a; Hadjimitrakis et al. 2007; Vidal et al. 1982).

After an SEF site was identified, control and stimulation trials were intermixed in equal probabilities. In both, a central red FP was provided directly in front of the monkey. The monkeys had to acquire the FP within 1,000 ms and hold gaze within a computer-controlled window (5°) between 750 and 1,250 ms. The FP was then removed. On stimulation trials, stimulation started 200 ms into the gap period and lasted for either 150–200 ms (head restrained) or 200–300 ms (head unrestrained). Once stimulation ended, a target was presented at one of eight different radial eccentricities (10° or 15° when head restrained, 15° or 20° when head unrestrained). On control trials, the duration of the gap interval between FP offset and target appearance matched that during stimulation trials. The monkeys had to maintain central fixation during the gap period on control trials, but this constraint was removed on stimulation trials after the onset of stimulation to account for the possibility of evoked saccades. The monkeys had 1,000 ms to look to the target within a computer-controlled window (radius 5°). All variables (i.e., fixation duration, trial type, target location) were presented an equal number of times within a block of ~60 trials in a pseudorandom order. The use of eight potential targets distributed radially around the central FP decreases the likelihood that the monkeys can prepare a specific saccade during the gap period (Basso and Wurtz 1997; Dorris and Munoz 1998).

Our protocol for acquiring and conditioning the EMG signals and for measuring gaze (eye-in-space) and head position (via a second coil secured to the head post in the frontal plane) has been described elsewhere (Elsley et al. 2007). A graphical user interface was designed to automatically detect the beginning and end of gaze shifts and head movements with velocity thresholds of 30°/s (gaze) or 10°/s (head) and display the data. These markers could be changed by an analyst, who could also reject trials for other reasons (e.g., excessive EMG activity due to postural shifts or head shakess). Anticipatory movements (beginning <60 ms from target appearance) or movements that began >600 ms after target appearance onset were automatically discarded. Trials with gaze shifts occurring just before or <20 ms after stimulation onset were also rejected. Trials were rejected at a rate of <5%.

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from a total of 215 unique sites (85 in monkey S and 130 in monkey Z) with standard stimulation parameters (300 Hz, 100 μA, duration 150–300 ms) and hence met our inclusion criteria: 115 of these sites were examined only with the head restrained, 50 of the sites were examined only in the head-unrestrained condition, and 25 of the sites were studied in both the head-restrained and head-unrestrained conditions.

The anatomical distribution of SEF sites was consistent with previous studies, being generally distributed ~2–5 mm from midline and between the caudal end of the arcuate sulcus and the rostral end of the superior arm of the arcuate sulcus (Chen and Walton 2005; Schall 1991b; Schlag and Schlag-Rey 1987). Almost all (99%) of the evoked gaze shifts had a contralateral component. We encountered a few caudal sites in previous studies, being generally distributed

Timing and metrics of evoked movements. SEF stimulation reliably evoked nontruncated gaze shifts from a central location in 55 sites that met our inclusion criteria (see METHODS; “nontruncated” refers to evoked gaze shifts that terminated even though stimulation was ongoing). Gaze shifts evoked from center spanned a large horizontal and vertical range regardless of head restraint (Fig. 1A). The radial magnitude of gaze shifts evoked with the head restrained was 13.3 ± 6.2° (range: 5–35°), angled at 31.1 ± 29.1° in the contralateral direction [range: −48° (down) to +71° (up)]. The radial magnitude of gaze shifts evoked with the head unrestrained was 22.0 ± 11.8° (range 2–45°) angled at 30.8 ± 32.5° [range: −25° (down) to +92° (up); 2 predominantly vertical head-free gaze shifts had a very small horizontal component ipsilateral to the side of stimulation]. Throughout our sample, the mean latency of gaze shift onset relative to stimulation was 92.4 ± 32.9 ms (range: 40–164 ms). With head unrestrained, initial eye-in-head, head-in-space, and eye-in-space positions were closely aligned in the horizontal plane (mean horizontal eye-in-head position = 1.4 ± 7.0°, mean horizontal eye-in-space = 0.25 ± 4.5°), with the head tilted upward slightly in the vertical plane (mean vertical eye-in-head position = −13.3 ± 5.1°, mean vertical eye-in-space = −0.4 ± 2.5°). From our head-unrestrained sample, the total amplitude of evoked head movements was 12.6 ± 6.7° (range: 0.8–35.8°) along the horizontal plane and 2.2 ± 1.9° (range: 0–6.3°) along the vertical plane. Head contribution (i.e., the size of the head movement during a gaze shift) was 3.5 ± 3.0° of the horizontal component (range: 0–13.1°) and 0.7 ± 0.8° of the vertical component (range: 0–2.7°). The mean of the evoked head movement onset was 72.5 ± 27.4 ms (range: 38–166 ms).

In monkey S, larger gaze shifts tended to be evoked from more anterior stimulation locations (Fig. 1A; linear regression of magnitude vs. anterior-posterior grid location, P = 0.001). Such a relationship was not observed in monkey Z. Neither the
magnitude nor the direction of evoked gaze shifts depended on stimulation location along the medio-lateral dimension.

We observed a number of relationships between the timing and metrics of head-unrestrained gaze shifts. First, we observed a positive correlation between evoked gaze shift magnitude and head contribution. Therefore, larger head contributions accompanied larger gaze shifts. Across our sample, the head started to contribute for evoked gaze shifts greater than \( \sim 10^{\circ} \) in amplitude. Second, the proportional head contribution to the gaze shift was typically larger the earlier the head began to move relative to gaze onset. Across our sample, head motion usually preceded the gaze shift. On such trials, the line of sight remained stable before the evoked gaze shift because of counterrotation of the eye within the head, but during the evoked gaze shift the eyes and head moved in the same direction at the same time. This pattern confirms that vestibular reflexes were modulated during eye-head gaze shifts evoked from the SEF. On trials with a saccadic gaze shift, the head had moved only \( 1.5 \pm 2.6^{\circ} \) in amplitude (range 0 to 21°), reaching a velocity of \( 27.0 \pm 34.6^{\circ}/s \) (range 0–192°/s) at the time of the gaze shift. Moreover, head velocity was \( <5^{\circ}/s \) on 32% of the gaze shifts evoked with the head unrestrained. Thus, although evoked gaze shifts could be associated with substantial head motion, it is clear that evoked gaze shifts are not a quick-phase response to head motion or to recenter eye-in-head position, as has been suggested for other forms of eye-head coordination (Barnes 1979; Guitton and Mandl 1980).

Finally, we also compared the velocity-amplitude main sequence relationships of head movements evoked by SEF stimulation to those accompanying volitional eye-head gaze shifts (Fig. 1B). For monkey S, the main sequence relationships for volitional and evoked movements overlapped. For monkey Z, the main sequence relationship for evoked head movements lay significantly below that for volitional movements.

Overall, the kinematics and timing of eye-head gaze shifts evoked by SEF stimulation resemble previous reports (Chen and Walton 2005; Martínez-Trujillo et al. 2003b), despite considerable differences in the behavioral paradigm and stimulation protocol. Having established this, we now turn to the analysis of evoked neck muscle responses and their relationships to evoked gaze shifts and/or head movements.

**Analysis of neck muscle EMG activity evoked by SEF stimulation.** Stimulation of the SEF results in substantial changes in neck muscle activity. The evoked responses consisted of the recruitment of a contralateral head turning synergy relative to the side of stimulation and a more variable recruitment of an upward or downward head pitching strategy. Given that the recruitment of the turning synergy was far more consistent, it is the primary focus of the ensuing analyses. We describe the more variable recruitment of upward or downward pitching strategies at the end of **RESULTS**.

Representative examples of neck muscle responses evoked by SEF stimulation are shown in Fig. 2. These examples demonstrate activity associated with medium (\( \sim 10^{\circ} \); Fig. 2, A and C)- or large (\( >20^{\circ} \); Fig. 2, B and D)-sized evoked gaze shifts. Figure 2, A and B, show data recorded from monkey S with the head restrained, after stimulation of two different SEF sites. At both sites, SEF stimulation evoked a rapid facilitation in the agonist neck muscles contralateral to the side of stimulation (contra-OCI, -RCM, and -SP). Such facilitation began shortly after stimulation (20–40 ms), peaked within the first 75 ms after stimulation onset, and then persisted at a plateau level until the end of stimulation. After cessation of stimulation, EMG activity quickly returned to baseline levels of activity prior to stimulation. These data are also ordered by increasing onset latency of the evoked gaze shift, demonstrating that the evoked neck muscle responses preceded evoked gaze shifts and persisted on trials without an accompanying gaze shift.

Figure 2, C and D, show example data recorded from the second monkey (monkey Z) when the head was unrestrained, selected to represent neck EMG activity associated with similarly sized gaze shifts. Although the absolute magnitudes of EMG recruitment are not directly comparable, we can make some general comparisons. A similar facilitation on the agonist muscles is apparent \( \sim 20 \) ms after stimulation onset when the head is unrestrained regardless of the size or presence of the ensuing gaze shift, as is the ensuing plateau of tonic recruitment that persisted until stimulation offset. In Fig. 2, C and D, head movements typically started \( \sim 40–75 \) ms after stimulation onset, usually well before the gaze shift. Similar to previous studies (Chen and Walton 2005), we occasionally observed trials consisting of evoked head movements without an accompanying gaze shift (Fig. 2, C and D); the eyes counterrotated in the head during such head-only movements to maintain gaze stability.

Although not shown in Fig. 2, SEF stimulation at these exemplar sites did not induce any recruitment in the ipsilateral turner muscles, relative to the side of stimulation. Instead, SEF stimulation appeared to decrease the activity on these muscles, although the observation of inhibition depended on the presence of background activity prior to stimulation. We observed robust inhibition of these muscles when background activity was present (see, for example, Fig. 3, A and B), which was synchronous with the facilitation of the contralateral agonist muscles.

In Fig. 2, E–H, we present the averaged EMG waveforms for the contralateral agonist muscles, segregated by whether SEF stimulation evoked an accompanying gaze shift or not. From these averaged waveforms, it is clear that the both the initial phasic response within the first \( \sim 75 \) ms and the ensuing tonic plateau for the remainder of stimulation persisted regardless of the presence or absence of an evoked gaze shift. However, both the initial peak and the subsequent plateau appeared to be slightly larger on trials with an accompanying gaze shift, particularly in the head-restrained examples.

In the analyses below, we quantify the facilitation latency and peak magnitude of the initial phasic response and the magnitude of activity during the tonic plateau (averaged over the last 100 ms of stimulation). It should be noted that because the tonic plateau could be confounded by either eye or head posture or motion, both of which can influence neck EMG activity, our analysis of the tonic plateau was derived only from those trials without any evoked movements.

**Influence of head restraint on evoked neck muscle responses.** Before proceeding with description of evoked neck muscle responses across our sample, we first examine the influence of head restraint. As mentioned above, 25 stimulation sites were studied with both the head-restrained and head-unrestrained conditions (data were collected with the head restrained first). Figure 3, A and B, shows an example of how the qualitative appearance of evoked neck EMG did not differ across head restraint (we also show an ipsilateral turner muscle here to
present an example of inhibition). Across our sample, we found that neither the facilitation latency nor the peak response of the phasic interval was influenced by head restraint (Fig. 3, C, and D). However, the magnitude of the plateau during the last 100 ms of stimulation was significantly greater with the head restrained across all muscles (Fig. 3E), even though this analysis was restricted to trials without evoked movements. Thus, head restraint only systematically influenced the tonic, not the phasic, recruitment component.

Quantification of evoked neck EMG responses from the SEF. For the ensuing analyses across our sample, we pooled the head-restrained and head-unrestrained data such that every data point represents a unique stimulation site. The data were combined from the 115 sites collected with the head restrained,
the 50 sites collected with the head unrestrained, and the 25 sites collected in both conditions (from these 25 sites, we only use data from the head-unrestrained condition). Across the 190 unique stimulation sites, EMG responses were evoked on the majority of trials, and this evoked activity frequently preceded the ensuing gaze shift. We also observed robust EMG activity even on trials without any accompanying gaze shift and/or head movement.

As with our exemplar data, SEF stimulation consistently evoked facilitation of the neck muscles contralateral to stimulation. Such contralateral muscle facilitation was never accompanied by any cocontraction of the ipsilateral turning muscles. Instead, SEF stimulation evoked a concomitant suppression of ipsilateral muscle activity when background activity was present. Thus the synergy evoked by SEF stimulation resembled the head turning synergy evoked by stimulation of the primate FEF (Elsley et al. 2007), SC (Corneil et al. 2002a), and INC (Farshadmanesh et al. 2008) and that seen during volitional head turns in the monkey (Corneil et al. 2001; Lestienne et al. 1995). We first constructed averages of evoked EMG activity by taking the mean stimulation-aligned waveform across all stimulation trials, with values collected with the head unrestrained plotted as a function of the values collected with the head restrained. Filled squares in D and E denote sites where significantly different responses were observed across head restrained (t-test, $P < 0.05$; site-by-site statistical testing in C was not possible as facilitation latencies are derived from the mean EMG waveforms and therefore do not have a variance). Diagonal line denotes the line of unity. Only the magnitude of the tonic plateau was influenced by head restraint ($P < 0.05$, 0.0001, and 0.0001 for OCI, RCP, and SP, respectively).

Evoked neck EMG responses tended to begin sooner and reach larger peak and plateau magnitudes when evoked from sites associated with larger gaze shifts (Fig. 4). The fact that stronger neck muscle recruitment that began sooner was evoked with progressively larger accompanying evoked gaze shifts presumably relates to the increasing head contributions for progressively larger gaze shifts. However, this analysis also shows that we commonly observed that significant evoked neck muscle responses accompanied relatively small gaze shifts $< 5^\circ$ in magnitude, even if this response was relatively weak and slow in developing. Thus, although the parameters of the evoked neck muscle response vary with the magnitude of the evoked gaze shift, SEF stimulation at sites evoking small gaze shifts that are not associated with overt head motion nevertheless still evoked a neck muscle response.

A final set of analyses examined whether expectancy of SEF stimulation influenced the background level of EMG activity
before stimulation onset. For example, perhaps the subjects were anticipating stimulation, or biasing initial positions in the direction of the evoked gaze shift. If so, this would confound the interpretation of the evoked response. Our first analysis took advantage of the fact that we stimulated both the left and right SEF in monkey S. Because of this, a given muscle would lie ipsilateral to the side of stimulation for some sites and contralateral to the side of stimulation at other sites. Across all the turner muscles implanted in monkey S, we observed no influence of the side of stimulation on the level of background EMG activity in the 100 ms prior to stimulation onset (Wilcoxon rank sum test; $P > 0.2$ for all 6 turner muscles). In a second analysis, we tested whether a possible anticipation of the magnitude of an accompanying gaze shift influenced background activity; if so, one would expect greater levels of background EMG on agonist muscles prior to larger gaze shifts. In both monkeys, we observed no systematic relationship between the level of background EMG activity and the ensuing gaze shift (linear regression, $P > 0.8$). While these analyses do not discount the possibility that the subjects are anticipating stimulation in some way, they demonstrate that any such anticipation did not influence neck EMG activity immediately prior to stimulation onset.

**Timing of evoked neck EMG responses relative to gaze onset.** We now examine the timing of evoked neck EMG responses relative to the timing of the evoked gaze shifts. As shown in Fig. 5, the site-by-site facilitation latencies on the contralateral turning muscles were universally shorter than the mean gaze shift onset (paired t-test, $P < 0.001$ for all muscles).

On average, facilitation latencies preceded gaze shifts by 65, 72, and 75 ms for OCI, RCP, and SP, respectively.

A shortcoming of the analysis reported in Fig. 5 is that it extracts EMG facilitation latency after averaging all stimulation trials, where the onset of gaze shifts are first determined on a trial-by-trial basis and then averaged. This could potentially overstate the difference between these EMG facilitation latencies and gaze shift onsets, as the former could be excessively influenced by trials that have a rapid onset. To address this problem, we performed a second analysis in which we determined the facilitation latency of EMG onset on a trial-by-trial basis, using an approach described elsewhere (Corneil et al. 2010; Elsley et al. 2007). Briefly, on each trial we constructed a cumulative EMG response across multiple muscles by adding the normalized increase in EMG activity from agonist muscles with the inverted normalized suppression of antagonist muscles (if present). The onset of an evoked response was determined when the level of this cumulative EMG response after activity exceeded 2 standard deviations from the average EMG activity of the 50 ms before stimulation.

The results for a single stimulation site are shown in Fig. 6A, which plots the facilitation latency from the cumulative EMG responses as a function of gaze shift onset on a trial-by-trial basis (using data from the site shown in Fig. 2B). From this individual site, it is apparent that EMG onset preceded gaze onset on almost every individual trial by at least 30 ms, and sometimes substantially longer.

We extended this analysis across our sample, comparing the relative onset of EMG activity with gaze onset in two different ways. First, for each stimulation site we plotted the mean EMG
.. stimulation trials, pooling across both monkeys and all were evoked (see Fig. 6). Timing and magnitude of evoked neck EMG responses relative to evoked head movement. Deriving the parameters of an evoked EMG response on a trial-by-trial basis permits us to compare these evoked responses to the parameters of the evoked head movement. Figure 7 shows a number of relationships between evoked EMG activity and the ensuing head movement, determined on a trial-by-trial basis. First, we compared mean EMG onset latencies against the mean head onset latencies across all stimulation sites. As expected, EMG activity reliably preceded head movements, both when averaged across stimulation sites (Fig. 7A; EMG responses lead head movements by 42 ± 28 ms) and when pooled across every single trial that had both an evoked EMG response and evoked onset latencies against the mean gaze onset latencies, both derived first on a trial-by-trial basis (Fig. 6B). To be included in this analysis, a minimum of 10 gaze shifts and 10 EMG responses had to be evoked from a single stimulation site. This analysis revealed that the mean onset of EMG activity is shorter than the mean onset of gaze, by 42.4 ± 25.8 ms. The mean EMG onset latencies also occurred before gaze onset in 94% (44/47) of sites that met our inclusion criteria. Furthermore, since trial-by-trial onsets for both measures can be derived, we can also measure the variability of each response. Figure 6C represents the relative timing of EMG and gaze onset, as well as the standard deviation of each measure. This plot again emphasizes that on a trial-by-trial basis EMG responses occurred prior to gaze shift onset on the majority of trials.

In our second trial-by-trial analysis, we compared the relative timing of the EMG and gaze shift onset across all stimulation trials where both a gaze shift and a neck muscle response were evoked (see Fig. 6D; pooling across both monkeys and all stimulation trials, n = 1,070). A histogram representing the lead time between EMG onset and gaze shift onset (EMG onset − gaze shift onset) shows that the EMG response preceded the gaze shift by 38.8 ± 31.2 ms, with negative values (where EMG onset preceded gaze onset) occurring on 87% of all trials. Overall, these results demonstrate conclusively that when stimulation was applied to the SEF, neck EMG responses almost always preceded the evoked gaze shift.

**Fig. 5.** Plot of facilitation latency as a function of the latency of evoked gaze shift for contralateral head turner muscles [OCI (A), RCP (B), SP (C)]. Each data point represents data taken from a unique stimulation site. All data clustered well below the line of unity (diagonal line), showing that facilitation latencies were far shorter than evoked gaze shift latencies (paired t-test, P < 0.001 for all 3 muscles).

**Fig. 6.** A: trial-by-trial plot of cumulative EMG onset latencies plotted as a function of evoked gaze onset latencies, taken from the site shown in Fig. 2B. Each square shows data from a single trial, and each × shows data from trials in which a gaze shift was not evoked (right). Data cluster below the line of unity (dashed diagonal line), showing that EMG onset latencies were shorter than gaze shift onset latencies here, by 37.3 ± 14.7 ms (paired t-test, P < 0.001). B: plot of mean EMG latency against mean gaze onset latency with both measures first determined on a trial-by-trial basis. Each square shows data taken from a single stimulation site, with filled squares denoting significant differences between mean onset EMG and mean onset gaze latencies (2-way t-test, P < 0.05). Clustering of data below the line of unity (dashed line) was significant (P < 0.001). C: plot of the relative timing of EMG onset vs. gaze onset with variance measures across all stimulation sites. Each point represents data taken from a single stimulation site, plotting relative timing of the EMG response vs. the gaze response (data were organized based on decreasing differences between these 2 measures). Positive values denote sites where gaze onset began before EMG onset. Horizontal error bars to the left or right of the black circles represent the SD of the EMG response or the gaze shift response, respectively, for each stimulation site. D: frequency histogram of the differences between EMG onset and gaze shift onset, determined on a trial-by-trial basis pooled across all stimulation sites. Positive values imply that the gaze shift response started before EMG onset. This distribution (−38.8 ± 31.3 ms, n = 1,070) is significantly below 0 (t-test, P < 0.001).
EMG activity on trials without evoked gaze shifts. Recall that our criteria for identifying a valid SEF site required that stimulation consistently evoke a gaze shift from any initial gaze position but our analysis of EMG activity was only derived when initial gaze position was straight ahead. Because of this, we frequently observed trials in which SEF stimulation failed to evoke a gaze shift. In fact, across all trials, SEF stimulation evoked a saccade only 35.4% of the time. As shown in Fig. 2, robust neck EMG responses persisted on trials without gaze shifts.

To quantify this observation, we compared EMG responses on trials with gaze shifts against trials with no gaze shifts. For this analysis, stimulation at a given site had to evoke a minimum of five trials either with or without an accompanying gaze shift. The results of this analysis are shown in Fig. 8, comparing both onset latency of the EMG response (Fig. 8A) and the peak of the initial response from the composite EMG response (Fig. 8B). This quantitative analysis of EMG response reveals that a significant neck EMG response was always observed on no-gaze trials (if no EMG response was recorded on no-gaze trials, points would fall along the x-axis). Second, there was no significant difference between the EMG onset latencies between gaze and no-gaze trials (paired t-test, \( P = 0.8 \); Fig. 8A). Third, the EMG response was slightly but significantly stronger on gaze trials compared with no-gaze trials, by 8.4 ± 25.2% (paired t-test, \( P = 0.03 \); Fig. 8B), even though this analysis was restricted to the period preceding a gaze shift. We repeated these analyses separately for data collected with the head restrained or unrestrained, and found no dependence with head restraint. Together, these results

Fig. 7. Comparison of parameters of evoked neck EMG response to the ensuing head movement. A: plot of mean EMG latency (determined on a trial-by-trial basis within a given stimulation site) as a function of mean onset of head movement. Each square shows data taken from a unique stimulation site, with filled symbols showing EMG responses that were significantly different from mean head movement onset (2-way t-test, \( P < 0.05 \)). Clustering of the data below the line of unity was significant (paired t-test, \( P < 0.001 \)), and EMG response latencies led head onset by 42 ± 28.4 ms. The regression (solid line) also reached significance (\( r = 0.63, P < 0.001, n = 45 \)). B: frequency histogram of the difference between EMG onset and head movement onset, determined on a trial-by-trial basis. Same format as Fig. 6D. This distribution (−37.7 ± 29.6 ms, median = −33 ms) is significantly distributed below 0 (t-test vs. 0, \( P < 0.001 \)). C and D: trial-by-trial correlations of either overall head movement amplitude (C) or peak head velocity (D) to the integral of the composite EMG response. This integral was calculated by taking the area under the EMG response curve for the duration of stimulation and subsequently normalized to the largest integral observed for each monkey. Regressions for both graphs were significant (C: Pearson’s \( r = 0.54, P < 0.001, n = 942 \); D: Pearson’s \( r = 0.55, P < 0.001, n = 942 \)).

head movement [Fig. 7B; EMG response preceded head movements by 37.7 ± 29.6 ms, with values less than −10 (i.e., EMG preceding head movement onset by >10 ms) occurring on 94% of trials]. For those individual trials that contained all of an EMG, head, and gaze response, the EMG activity was best aligned to stimulation onset (27.8 ± 19.7 ms, \( n = 449 \)) compared with either the onset of the gaze shift (−69.4 ± 41.4 ms) or the head movement (−41.4 ± 37.2 ms). On these trials, the head movement preceded the gaze shift by 28.0 ± 50.7 ms.

We also compared the magnitude of EMG recruitment to the kinematics of evoked head movements. We constructed the normalized integral of the composite EMG response on a trial-by-trial basis and plotted these values against head amplitude (Fig. 7C) and peak head velocity (Fig. 7D). As expected, the cumulative EMG response was a strong predictor of both head amplitude and peak head velocity (\( r = 0.54, P < 0.001 \) and \( r = 0.55, P < 0.001 \), respectively; the fit of EMG data to peak head velocity improved slightly if we integrated EMG activity in the 50 ms after response onset, capturing the initial phasic response), consistent with the evoked neck EMG response driving the subsequent evoked head movement.

Fig. 8. Comparison of evoked EMG responses on trials with or without accompanying evoked gaze shifts (labeled gaze and no-gaze trials, respectively), contrasting the EMG onset latency (A) and the peak of the initial response from the composite EMG response (arbitrary units (a.u.), B). Each square was taken from a unique stimulation site, with filled squares representing sites that were significantly different from each other (2-way t-test, \( P < 0.05 \)). Integral data were normalized to maximal integral recorded within each monkey. Across our sample, the magnitude of the EMG response was significantly larger on gaze trials, but the response latency did not differ significantly (paired t-test, \( P = 0.02 \) and \( P = 0.8 \), respectively).
suggest that SEF recruitment of the neck musculature occurs even in the absence of an overt gaze shift, with the evoked neck muscle response reaching greater magnitude on trials with an accompanying gaze shift.

**Head movement parameters on stimulation trials without a gaze shift.** Our description of EMG activity in the absence of gaze movements suggests that SEF stimulation in the head-unrestrained condition has the potential to drive orienting head movements without a gaze shift. As reported by Chen and Walton (2005), we also observed a number of sites from which stimulation could evoke either an eye-head gaze shift or a head-only movement (gaze remained stable during head-only movements due to because of a compensatory vestibulo-ocular reflex). Here, we compare trials in which stimulation evoked a head-only movement to those with an evoked eye-head gaze shift.

To analyze such head movements across our sample of SEF sites examined in the head-unrestrained condition, we identified sites from which stimulation evoked at least five eye-head gaze shifts (termed gaze trials) and five head-only movements (termed no-gaze trials). Of our 76 head-unrestrained sites, 28 unique sites matched these criteria. Our analysis then compared evoked head movements on trials with or without an accompanying gaze shift and revealed that a larger head movement was evoked in trials that had an accompanying gaze shift (Fig. 9A; paired t-test, *P < 0.001*). In addition, the head also moved faster when accompanied by a gaze shift (Fig. 9B; paired t-test, *P < 0.001*). However, the timing of head movement onset did not differ on trials with or without an accompanying gaze shift (results not shown; paired t-test, *P = 0.37*). Our analysis on the composite EMG activity demonstrated that the peak magnitude of the initial EMG response was also greater on gaze trials, by 15.8 ± 29.3% (Fig. 9C; paired t-test, *P < 0.01*), even though the onset of EMG activity did not differ in trials with or without a gaze shift (results not shown); paired t-test, *P = 0.77*). Thus greater neck EMG responses and larger and faster head movements were evoked on trials with an accompanying gaze shift.

**Subtle head movements on trials without overt head motion.** Although SEF stimulation evoked neck muscle responses on almost all trials, such recruitment was not necessarily accompanied by overt head motion that exceeded our detection criteria. Given the head’s substantial inertia, and reports describing subtle head motion far below traditional detection criteria (Chapman and Corneil 2011; Oommen and Stahl 2005), we conducted more precise analyses of head position and velocity on trials without overt head motion. These analyses directly compared head movement parameters during SEF stimulation with those during the same time interval on control trials without stimulation. In Fig. 10A, we show an example of head position and velocity during either control or stimulation trials. Despite the failure to detect overt head motion on a trial-by-trial basis in the latter, it is clear that SEF stimulation is causing a very small (<2°) and slow (<10°/s) head movement; an examination of eye velocity reveals the presence of compensatory eye motion. To study such motion more quantitatively, we produced a time series receiver operating characteristics analysis (ROC; see Chapman and Corneil 2011 for details), comparing head velocity on trials with or without stimulation. This analysis reveals that an ideal observer could have discriminated stimulation from control trials ∼35 ms after stimulation onset, based solely on head movement velocity (Fig. 10A, bottom; our criterion for this site-by-site analysis was the first of 10 consecutive time points with ROC values exceeding 0.75).

We repeated this analysis across our sample of all head-unrestrained stimulation sites, directly comparing the head velocity across stimulation and control trials for those sites where overt head motion was not detected on at least five trials (sufficient trials were obtained from 30 stimulation sites). From this subset, the ROC analysis on head velocity discriminated stimulation from control trials in 23 sites, with discrimination times averaging 84 ± 41 ms (Fig. 10B; range: 35–207 ms). We also conducted another analysis after collapsing our data across our sample of head-unrestrained sites, pooling control and stimulation trials (the latter without detected head motion) across all head-unrestrained stimulation sites. This produced a data set of 1,391 control trials and 479 stimulation trials, and while there was negligible head motion on control trials, stimulation clearly produced a very slow head movement that peaked at ∼5°/s (Fig. 10C). A time-series ROC analysis on head velocity produced a discrimination time of 71 ms (Fig. 10C; our criterion for this analysis collapsed across our
Fig. 10. Subtle head motion on trials without detected head motion. A: example site comparing horizontal head position (HH; showing individual traces) and horizontal head and eye velocity (dHH and dEH; mean sub tended by standard error) on control trials (black traces) and stimulation trials (gray traces, including only those stimulation trials where an overt head movement was not detected). Bottom: time series receiver operating characteristic (ROC) analysis comparing head velocity on control and stimulation trials, with the resulting discrimination time. B: frequency histogram of discrimination times obtained from 23 of 30 stimulation sites with at least 5 trials without head motion. C: top: horizontal head velocities (mean sub tended by SE) of control trials or stimulation trials without detected head motion, pooled across all head-unrestrained stimulation sites. Bottom: time series ROC analysis for comparison of these head velocities. See accompanying text for details on ROC discrimination times.

sample was the first of 10 consecutive points with ROC values exceeding 0.6, given the far greater number of trials.

These analyses demonstrate that the head motion arising from SEF stimulation can be quite subtle; evidence for such motion emerged only after stimulation trials were pooled together and compared with control trials without stimulation.

Comparison of evoked neck muscle responses to those accompanying volitional head movements. Stimulation of the SEF evokes eye-head gaze shifts that appear kinematically similar to volitional movements (Martinez-Trujillo et al. 2003b). Here, we sought to compare whether the profile of neck muscle recruitment following SEF stimulation resembles that observed during volitional head movements made during control trials. Unfortunately, this comparison is somewhat limited given our behavioral paradigm, in which targets were placed at one of eight radially distributed potential locations (see Methods); we made no effort to try to match the kinematics of evoked head movements with those made during volitional eye-head gaze shifts made to look at the target (see Monteon et al. 2010 for a recent example of such kinematic matching). Therefore, we focused on stimulation sites where the evoked gaze shift vector brought the final gaze position within 2.5° (head restrained) or 3.5° (head unrestrained) of one of the target locations lying contralateral to the side of stimulation. In Fig. 11A, we show a representative example of EMG data aligned to either evoked gaze shift onset (Fig. 11A, top) or a volitional eye-head gaze shift (Fig. 11A, bottom). This example shows that EMG activity attained a visibly larger magnitude on stimulation trials. In contrast, the EMG activity during control trials was far more modest, with negligible amounts of activity prior to gaze shift onset. These trends persisted across our sample data, with EMG activation on all three turner muscles being greater on stimulation versus control trials (see Fig. 11B). Although limited, this analysis suggests that the profile of neck muscle recruitment reaches a greater magnitude during evoked versus volitional gaze shifts.

Evoked neck muscle responses on extensor muscles. Up until now, we have focused on evoked responses on neck muscles primarily associated with horizontal head turns. However, SEF stimulation commonly evoked responses bilaterally on the extensors muscles BC and COM. In Fig. 12, we present EMG activity from both muscles accompanying a head-restrained evoked gaze shift with a large upward component. Here, SEF stimulation evoked bilateral facilitation of both BC and COM. Similar to the head turner muscles, EMG activity on the extensors occurred before the gaze shift, remained throughout stimulation duration, and persisted on trials without an evoked gaze shift.

Across our sample, the facilitation latencies for extensor muscles (see Fig. 13A) tended to be similar when compared with the turner muscles (Fig. 3). The mean facilitation latencies for contra-BC, contra-COM, ipsi-BC, and ipsi-COM were 28.4 ± 13.8 ms (median = 25 ms), 35.4 ± 15.2 ms (median = 35 ms), 36.1 ± 17.3 ms (median = 36 ms), and 38.6 ± 17.7 ms (median = 35 ms), respectively. The facilitation latencies for contra-BC tended to be larger for gaze shifts with larger vertical components but surprisingly invariant across the other three muscles. Larger peak magnitudes were associated with gaze shifts with larger upward gaze components on the ipsilateral extensors; however, this relationship was not observed on the contralateral extensors (Fig. 13).

DISCUSSION

We have described neck EMG evoked by stimulation of the monkey SEF. Stimulation of the SEF occasionally evoked overt contralateral gaze shifts and/or head movements but almost always evoked a contralateral head turning synergy. This evoked response consisted of an initial phasic response followed by a more sustained plateau of tonic recruitment. Evoked neck muscles responses began well in advance of evoked movements (~40–70 ms), scaled with evoked movements, accompanied even small movements, and persisted on trials without an accompanying gaze shift or overt head movement. Overall, the parameters of neck muscle responses evoked by SEF stimulation, and the relationship of such responses to evoked gaze shifts and/or head movements, are comparable to neck muscle responses evoked by FEF stimulation (Cornel et al. 2010; Elsley et al. 2007), emphasizing similar contributions of frontal oculomotor structures to orienting head movements. However, the latency of the neck muscle responses evoked from the SEF is substantially longer, consistent with a hierarchy in which the SEF is further removed from the motor periphery compared with the FEF.
Comparison to previous SEF studies. In their seminal work identifying the monkey SEF, Schlag and Schlag-Rey (1987) reported stimulation-evoked head movements in only 1 of 10 sites, even with prolonged stimulation up to 1 s in duration. These observations led them to suggest that the SEF was not primarily involved in the control of head movements, as suggested in much earlier work (Brown 1922; Levinsohn 1909; see Chen and Tehovnik 2007 for review). Instead, they proposed an oculomotor role for the SEF, similar to the nearby FEF. In agreement with this, many aspects of the evoked neck muscle responses resemble those evoked by FEF stimulation (see below). However, we were struck by how commonly SEF stimulation evoked a neck muscle response (in ~95% of all stimulation sites); more recent work by Martinez-Trujillo and colleagues (2003b) and Chen and Walton (2005) also reported a proportion of sites from which head movements were not consistently evoked (33% and 18%, respectively). While the results from these previous SEF reports would seem consistent with a mosaic intermixing of eye-alone, eye-head, or head-alone sites, we saw little evidence for this from the perspective of evoked neck muscle activity. Instead, we favor the interpretation that the command resulting from SEF stimulation is a general orienting command. The expression of this orienting command as a neck muscle response, an overt head movement, and/or a gaze shift depends on numerous factors including the initial position of the eyes and head (recall our criteria for identifying SEF sites; see also Chen and Walton 2005) and whether the consequent forces arising from the neck muscle response can overcome the head’s inertia to produce detectable head motion. In this regard, we suspect that many of the sites classified in earlier studies as not evoking a head movement would have evoked a neck muscle response had it been measured. The surprisingly low number of stimulation sites reported by Schlag and Schlag-Rey (1987) may also have arisen from a limited study of SEF stimulation sites associated with particularly small, vertically
movements from center beginning (pointed straight forward) and observed a strong influence of the head (e.g., gaze pointing to the right while the head is systematically dissociate the relative orientation of the eye and stimulation onset. Chen and Walton (2005) trained monkeys to respectively), our monkeys were looking straight ahead prior to 90 and $/H_1\text{H}_11011$ onset, respectively. While these response latencies are shorter head movements began (Martinez-Trujillo et al. 2003a, 2003b, 2004). Gaze shifts and stimulation were delivered after monkeys arrived at the location of a evoked compare favorably to these other reports. In the studies and Walton 2005; Martinez-Trujillo et al. 2003b). Despite more to horizontal gaze shifts (Freedman and Sparks 1997)] as our results are consistent with more recent results showing that SEF stimulation readily evokes orienting head movements both in conjunction with and independent of gaze shifts (Chen and Walton 2005; Martinez-Trujillo et al. 2003b). Despite considerable differences in the behavioral paradigm and stimulation parameters, the kinematics of the movements that we evoked compare favorably to these other reports. In the studies conducted by Martinez-Trujillo and colleagues, stimulation was delivered after monkeys arrived at the location of a previously flashed stimulus placed throughout the visual field (Martinez-Trujillo et al. 2003a, 2003b, 2004). Gaze shifts and head movements began 40 ms and 55 ms after stimulation onset, respectively. While these response latencies are shorter than what we observed (~90 and ~70 ms for gaze and head, respectively), our monkeys were looking straight ahead prior to stimulation onset. Chen and Walton (2005) trained monkeys to systematically dissociate the relative orientation of the eye and the head (e.g., gaze pointing to the right while the head is pointed straight forward) and observed a strong influence of initial head position on movement onset latencies, with head movements from center beginning ~125 ms after stimulation.

Chen and Walton (2005) also found that head movement amplitude increased with longer stimulation duration. This finding likely relates to our neck EMG recordings showing an initial peak of activation followed by a sustained plateau of recruitment that persisted for the duration of stimulation.

**Influence of cognitive state and head restraint.** The SEF is recognized as an interface between cognition and action, providing a plausible substrate by which cognitive goals can shape ensuing movements (Nachev et al. 2008). SEF activity is influenced by task set, and the behavioral state adopted at the time of SEF stimulation can influence the evoked movements (see, e.g., Chen and Walton 2005; Tehovnik et al. 1999). Although we designed our task to specifically prevent the monkeys from being able to predict target location, could behavioral factors have influenced the profiles of evoked neck muscle activity? For example, the subjects may be anticipating the possibility of stimulation, which could influence neck muscle recruitment even before stimulation onset. Two observations are not consistent with this scenario. First, the background level of neck EMG activity in a given muscle in monkey S was the same regardless of whether stimulation was delivered to the right or left SEF. Second, in either subject, this background level of neck EMG did not relate in any way with the size of the evoked movement in either monkey.

While these analyses of background activity are not consistent with a role of anticipation, the initial evoked neck muscle response reached a greater magnitude on trials in which an ensuing movement would be evoked (Figs. 8, 9). This result may be explained by trial-by-trial fluctuations in the vigilance with which the animal is maintaining fixation, since the probability of an evoked saccade decreases during active fixation (Tehovnik et al. 1999). Thus it appears that the comparative magnitude of the evoked neck muscle response can be influenced by the behavioral state of the animal. Future studies utilizing more complex paradigms known to recruit the SEF are required to specifically address the influence of the behavioral state on the evoked cephalomotor command.

**Comparison to previous studies in other areas.** A series of studies have paired stimulation with the recording of neck muscle activity in the primate or feline FEF (Corneil et al. 2010; Elsley et al. 2007; Guitton and Mandl 1978), SC (Corneil et al. 2002a, 2002b, 2007; Guitton et al. 1980; Hadjidimitrakis et al. 2007; Roucoux et al. 1980), and INC (Farshadmanesh et al. 2008). As with each of these areas, stimulation of the SEF resulted in the rapid recruitment of a contralateral head turning synergy that scales with the magnitude of any accompanying gaze shift. Neck muscle responses evoked from all areas also consisted of a phasic initial response followed by a more sustained plateau of recruitment. Given that our monkeys performed a task identical to that in the FEF study of Elsley and colleagues (2007), we can directly compare many aspects of our results. With the exception of the latency of the evoked response, virtually all of the results reported here were also observed in the FEF. These similarities suggest that efferent projections from the SEF ultimately access the same brain stem and spinal orienting circuits as those accessed after FEF stimulation.

The main difference between neck muscle responses evoked from the SEF or FEF is in the response latencies relative to stimulation. Neck muscle latencies following stimulation of the primate FEF stimulation are ~17 ms (Elsley et al. 2007), those
following SC stimulation are \(\sim 13\) ms in the monkey (Corneil et al. 2002a) or \(\sim 8\) ms in the cat (Hadjidimitrakis et al. 2007), and those following stimulation of the primate INC are \(\sim 10\) ms (Farshadmanesh et al. 2008). These values approach the minimal synaptic and conduction delays from the stimulated area to the motor periphery, suggesting that stimulation in each of these structures initiates sufficient activity along efferent projections to produce rapid propagation through polysynaptic relays in the brain stem and spinal cord (see Elsley et al. 2007 for detailed consideration of timing and possible pathways from the FEF). We accordingly speculate that the initial phasic response to stimulation of the FEF, SC, or INC is a feedforward response unaffected by reafference.

Neck muscle responses from the SEF averaged 30 ms, which is substantially longer than one might expect if the signal was relayed first through the FEF, SC, and/or pontomedullary reticular formations before accessing premotor centers in the brain stem and spinal cord. This result parallels the findings of Schlag and Schlag-Rey (1987) that saccadic response latencies to SEF stimulation are considerably longer than those evoked from the FEF. The longer neck muscle response latency to SEF compared with FEF stimulation may be due to the absence or coarseness of any topographic representation of motor commands in the SEF (we observed a coarse topography in one monkey but not the other). SEF efferents are also distributed more widely throughout the SC than efferents from the FEF (Huerta and Kaas 1990; Shook et al. 1990), suggesting a more diffuse pattern of projections onto subcortical targets. It also appears that the density of saccade-related neurons is higher in the FEF than the SEF (Tehovnik and Sommer 1997). Finally, there is no guarantee that the current level used in this study (100 \(\mu\)A) equates to that used in the complementary study of the FEF (50 \(\mu\)A), and neck EMG response latencies increase as stimulation currents are lowered relative to saccade threshold (Corneil et al. 2010; Hadjidimitrakis et al. 2007). Taking these factors together, we suggest that signals evoked by SEF stimulation take longer to propagate through to the motor periphery because the consequent efferent drive is weaker and less focal than that evoked by FEF stimulation, increasing the delays required for temporal and spatial summation at each stage within a polysynaptic pathway. Despite these increased delays, we speculate that the initial phasic response to SEF stimulation is essentially still a feedforward response.

Influence of head restraint on tonic component of evoked neck muscle response. Although head restraint did not systematically influence the timing and magnitude of the initial neck muscle response, the magnitude of the ensuing tonic plateau was greater with the head restrained (Fig. 3). This finding suggests that feedback can influence the evoked neck muscle response, but the nature and origin of this feedback signal remain unclear. Recall that we restricted the analysis of the plateau to trials without evoked movements to avoid confounds between neck EMG and eye-in-head or head-on-body position; hence the influence of head restraint on the plateau cannot be explained by differences in positional or kinematic parameters or vestibulospinal reflexes. At the present time, it is unclear whether this result is particular to SEF stimulation or arises as a consequence of head restraint. The deep dorsal neck muscles have a particularly rich complement of proprioceptive organs (Cooper and Daniel 1963; Richmond et al. 1999). Although the monosynaptic stretch reflex is much weaker than in limb muscles (Keirstead and Rose 1988a, 1988b), there are numerous polysynaptic spinal and supraspinal routes (e.g., via the central cervical nucleus or vestibular nuclei) by which reafferent information from neck muscles can influence descending motor commands (see Richmond et al. 2001a for review). Afferent neck muscle information also influences activity in numerous cortical and subcortical oculomotor targets (Fukushima et al. 2010; Nagy and Corneil 2010; Snyder et al. 1998). While the divergence of these ascending projections provides ample opportunity for interaction with descending motor commands, the nature of these interactions, and why they are influenced by head restraint, remains unclear. A comparison of the phasic and tonic components of neck muscle activity evoked by stimulation of the SEF, FEF, SC, and INC would be fruitful in helping to differentiate site-specific versus peripheral mechanisms.

**Comparison to natural orienting head movements.** Although limited by the behavioral paradigm, we found that neck muscle activity achieved greater levels of activity following SEF stimulation than observed during volitional eye-head gaze shifts. This finding is similar to that made after stimulation of either the SC or FEF (Corneil et al. 2002b; Elsley et al. 2007). Thus while eye-head gaze shifts evoked from the SEF, FEF, or SC appear kinematically normal (Freedman et al. 1996; Martinez-Trujillo et al. 2003b; Monteon et al. 2010), the underlying mechanisms appear not to be the same.
ing profile of neck muscle recruitment is quite different. The kinematic similarities between evoked and volitional head movements likely arise because of the low-pass filtering characteristics imposed by the head’s inertia. Possible pathways mediating cephalomotor responses from the SEF. Anatomical studies suggest a number of alternatives for how a command evoked by SEF stimulation can get to oculomotor and cephalomotor structures. The SEF has connections with numerous cortical oculomotor areas including the FEF and also projects to the intermediate and deep layers of the SC, the caudate, and other targets within the brain stem (Huerta and Kaas 1990; Parthasarathy et al. 1992; Schall et al. 1993; Shook et al. 1990, 1991). Such diverse projections, when considered alongside the prolonged neck muscle response latencies we have observed (particularly compared with the FEF), hinder our ability to draw conclusions about the pathway or pathways mediating the evoked neck muscle responses. For example, are the FEF and/or SC required? Tehovnik and colleagues (Tehovnik et al. 1994) reported that saccades could still be evoked from the SEF after ablation of either the SC or the FEF, but it is unknown whether this result is due to pathways projecting from the SEF to the oculomotor brain stem or due to the integrity of the remaining FEF or SC, respectively. Regardless of how the signals evoked by SEF stimulation access oculomotor and cephalomotor circuits (i.e., whether via the FEF or SC or directly to brain stem premotor circuits and then onto the eye or head plant), their expression in the motor periphery is very similar to that following FEF, SC, or INC stimulation. Comparative timing of cephalomotor versus oculomotor responses. Recordings of neck muscle activity are endowed with a high temporal resolution, essentially on a millisecond scale. Regardless of whether neck muscle response latencies were determined after stimulation-aligned averaging or on a trial-by-trial basis, cephalomotor responses led saccadic gaze shifts by ~40–70 ms when both responses were present. Although we did not measure EMG activity on extraocular muscles in this study, the delay between the activation of extraocular motoneurons and the onset of eye motion is only ~8 ms (Fuchs and Luschei 1970), meaning that recruitment of neck muscle motoneurons likely leads that of extraocular motoneurons by at least ~30 ms. This is quite a substantial delay, and even greater than that arrived at by similar considerations of timing from the FEF, where neck muscle recruitment is estimated to lead extraocular muscle recruitment by ~10–15 ms (Elsley et al. 2007).

This line of thinking leads to speculation on the mechanisms governing the initiation of cephalomotor versus oculomotor commands. Given the similarities of our results to those evoked from the SC and FEF, it is tempting to speculate that the relevant mechanisms reside downstream of the SC, in the brain stem and/or spinal cord. In Elsley et al. (2007), we suggested that brain stem omnipause neurons (OPNs) selectively delay the expression of oculomotor responses to FEF stimulation without imposing a similar delay on cephalomotor commands. The notion that OPNs exert their inhibitory influence selectively on premotor oculomotor but not cephalomotor components is consistent with a host of conceptual models and neurophysiological results (Corneil et al. 2004, 2010; Galiana and Guitton 1992; Gandhi and Sparks 2007; Goossens and Van Opstal 1997; Pélishon et al. 2001; Phillips et al. 1995; Rezvani and Corneil 2008). Briefly, such selective inhibition means that higher levels of activity are required to initiate gaze shifts than orienting head movements.

The hypothesized selective inhibition of OPNs on oculomotor but not cephalomotor premotor circuits provides a plausible way of delaying oculomotor versus cephalomotor commands. However, the processing of signals relayed via descending pathway (e.g., tecto-reticulo-spinal, interstitiospinal, or vestibulospinal pathways) motor commands in the upper cervical spinal cord remains unclear. Numerous anatomical studies have shown that these descending motor systems ramify into both the intermediate zones and ventral horn of upper cervical segments, providing both direct and indirect (via spinal interneurons) routes to influence neck muscle recruitment (e.g., Cowie et al. 1994; Sugiuichi et al. 2004; see Isa and Sasaki 2002 for review). While these pathways appear to provide a substrate for the hardwiring of different neck muscle synergies (Sugiuichi et al. 2004), the role played by cervical spinal circuits in the elaboration of neck muscle recruitment during behavior remains unclear. This area appears inaccessible to conventional neurophysiology, as current techniques for recording in the lower cervical spinal column (Perlmutter et al. 1998) require fusion of cervical vertebrae and would damage many of the neck muscles of interest.

Summary. The SEF has been implicated in high-level processes that link abstract rules to action. Although the SEF is undoubtedly a higher-level structure than the FEF, the results presented here show that SEF stimulation almost invariably recruits a contralateral head turning synergy. This basic description lays the groundwork for future studies investigating how this evoked response varies with experimental manipulations of initial eye and head position or task context. No one pattern of eye-head coordination is uniquely used for isometric gaze shifts. Instead, eye-head coordination can be influenced by numerous low- and high-level processes. Our results demonstrate that the SEF has short-latency access to cephalomotor circuits; hence the SEF is a likely candidate for instantiating such high-level control.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: B.B.C. and B.D.C. conception and design of research; B.B.C., M.A.P., and S.L.C. performed experiments; B.B.C., M.A.P., and S.L.C. analysed data; B.B.C., M.A.P., and B.D.C. interpreted results of experiments; B.B.C. and B.D.C. prepared figures; B.B.C. and B.D.C. drafted manuscript; B.B.C., M.A.P., S.L.C., and B.D.C. edited and revised manuscript; B.B.C. and B.D.C. approved final version of manuscript.
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